Growth Regulatory Pathway collaborates with Axial Patterning Genes to regulate Patterning and Growth in *Drosophila Eye*

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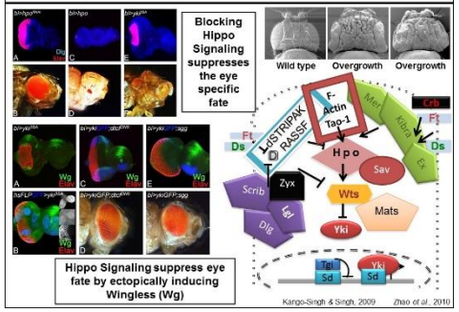
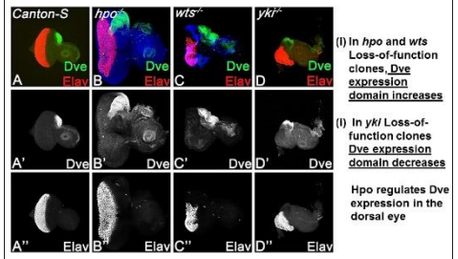
Abstract

In any multicellular organism, organogenesis requires axial patterning to determine Antero-Posterior (AP), Dorso-Ventral (DV), Proximo-Distal (PD) axes. Any deviation in these axes during development leads to congenital birth defects. In our model system, *Drosophila melanogaster* (a.k.a fruit fly), Dorso-Ventral (DV) patterning marks first lineage restriction event. We have identified *defective proventriculus* (*dve*- a Homeobox gene), an ortholog of SATB homeobox 1 (special AT-rich sequence binding protein 1), as a new member of DV patterning gene hierarchy. We have shown that *dve* acts downstream of *pannier* (*pnr*, GATA-1 transcription factor), and upstream of *wingless (wg)* in dorsal gene hierarchy. Loss-of-function of *dve* or *pnr* results in dramatic dorsal eye enlargements, whereas gain-of-function suppresses the eye fate. We have demonstrated that Wg is a downstream target of Hippo growth regulatory pathway (highly conserved) in eye. Furthermore, Wingless (Wg), which acts downstream of *dve*, also exhibits similar eye enlargement and suppression phenotypes and has been shown to play a role in growth. Here, we present that DV patterning genes interact with Hippo signaling to regulate the common downstream target, Wg during growth and patterning of developing *Drosophila* eye. Our data (using Gain-of-function studies) states that activation of Hippo signaling in *dve*, *pnr* expression domain results in change of head specific fate to an eye. We have tested retinal determination fate markers in these backgrounds. This study will address an important question, whether the axial patterning genes (*dve*, *pnr*) and Hippo pathway regulates patterning and growth independently or in-coordination with each other by regulating Wg signaling in order to form an eye/or any organ. The results from these studies will be presented.

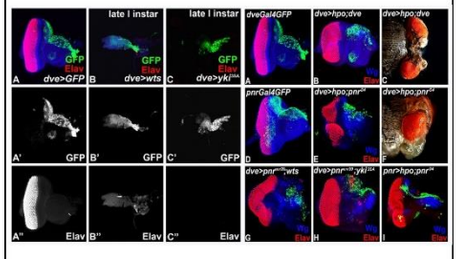
Loss-of-function of Hippo pathway exhibits growth phenotypes



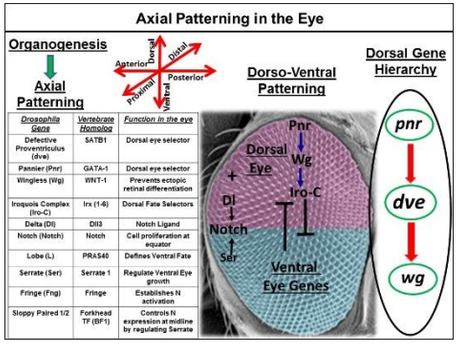
LOF of Hippo Signaling ectopically induces Dve expression in eye



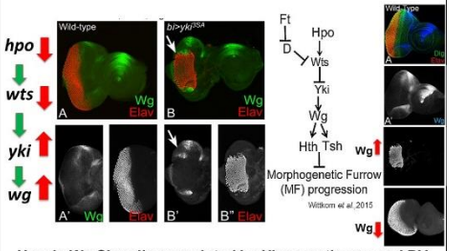
Hippo pathway members acts upstream of DV patterning genes



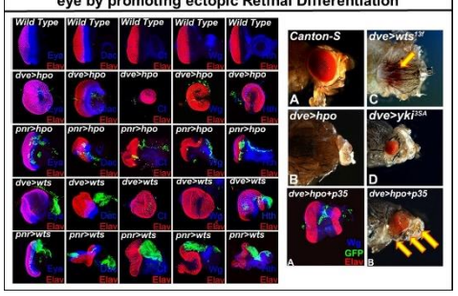
Axial Patterning in the Eye



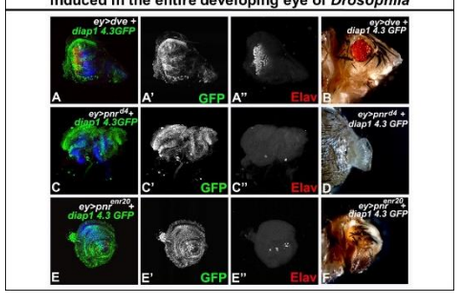
Wingless is the downstream target of Hippo pathway in eye



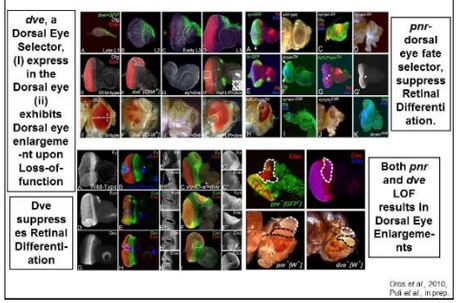
Activating Hippo Signaling suppresses *dve*, *pnr* expression, modulates Wg & transforms head, antenna cells fate to an eye by promoting ectopic Retinal Differentiation



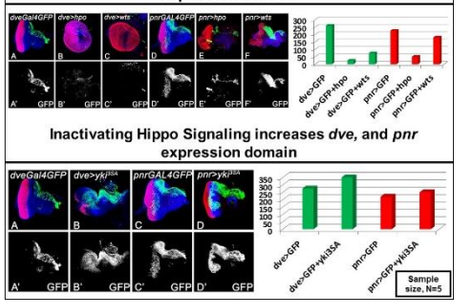
Downstream target of Hippo pathway, Diap1 expression in eye gets upregulated when *pnr* and *dve* expression is induced in the entire developing eye of *Drosophila*



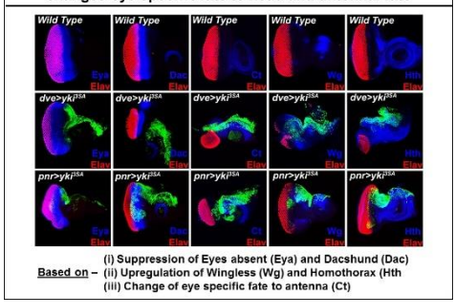
Loss-of-function of *dve*, and *pnr* exhibits growth phenotypes



Activating Hippo Signaling reduces *dve*, and *pnr* expression domain

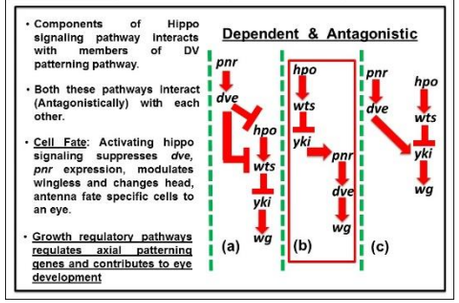


Inactivating Hippo Signaling in *dve* or *pnr* expression domain changes eye specific fate to head and antennal fate



Conclusions

- Components of Hippo signaling pathway interacts with members of DV patterning pathway.
- Both these pathways interact (Antagonistically) with each other.
- Cell Fate: Activating hippo signaling suppresses *dve*, *pnr* expression, modulates wingless and changes head, antenna fate specific cells to an eye.
- Growth regulatory pathways regulates axial patterning genes and contributes to eye development



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